

09/7/16, 054  
L/Cook 4/7/05.  
updated Search.

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(FILE 'HOME' ENTERED AT 10:43:35 ON 07 APR 2005)

FILE 'BIOSIS, CAPLUS, EMBASE, MEDLINE, CANCERLIT, JAPIO' ENTERED AT  
10:43:50 ON 07 APR 2005

L1 280259 S (PROTEIN BINDING)  
L2 28145 S L1 AND (IN VIVO)  
L3 917 S L2 AND REVIEW?  
L4 317 S L3 AND INHIBIT?  
L5 148 S L4 AND CLINICAL?  
L6 127 DUPLICATE REMOVE L5 (21 DUPLICATES REMOVED)  
L7 0 S L6 AND FKBP?  
L8 573 S L1 AND FKBP?  
L9 66 S L8 AND L2  
L10 3 S L9 AND REVIEW?  
L11 1 DUPLICATE REMOVE L10 (2 DUPLICATES REMOVED)

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RESERVED. on STN

AN 2004031151 EMBASE

TI Adaptor protein interactions: Modulators of amyloid precursor protein metabolism and Alzheimer's disease risk?.

AU King G.D.; Turner R.S.

CS R.S. Turner, Geriatr. Res., Educ., and Clin. Ctr., Veterans Affairs Healthcare System, 2215 Fuller Road, Ann Arbor, MI 48105, United States.  
raymond.t@umich.edu

SO Experimental Neurology, (2004) Vol. 185, No. 2, pp. 208-219.

Refs: 154

ISSN: 0014-4886 CODEN: EXNEAC

CY United States

DT Journal; General Review

FS 005 General Pathology and Pathological Anatomy

008 Neurology and Neurosurgery

037 Drug Literature Index

038 Adverse Reactions Titles

LA English

SL English

ED Entered STN: 20040212

Last Updated on STN: 20040212

AB The cytoplasmic C-terminus of APP plays critical roles in its cellular trafficking and delivery to proteases. Adaptor proteins with phosphotyrosine-binding (PTB) domains, including those in the X11, Fe65, and c-Jun N-terminal kinase (JNK)-interacting protein (JIP) families, bind specifically to the absolutely conserved -YENPTY- motif in the APP C-terminus to regulate its trafficking and processing. Compounds that modulate APP-adaptor protein interactions may **inhibit** A $\beta$  generation by specifically targeting the substrate (APP) instead of the enzyme ( $\beta$ - or  $\gamma$ -secretase). Genetic polymorphisms in (or near) adaptor proteins may influence risk of sporadic AD by interacting with APP **in vivo** to modulate its trafficking and processing to A $\beta$ . .COPYRGHT. 2003 Elsevier Inc. All rights reserved.

CT Medical Descriptors:

\*Alzheimer disease: ET, etiology

protein protein interaction

protein metabolism

risk factor

protein expression

amino acid sequence

protein synthesis

protein function

**enzyme inhibition**

carboxy terminal sequence

protein degradation

protein secretion

protein motif

molecular cloning

protein transport

**protein binding**

protein domain

sequence homology

protein family

amino terminal sequence

two hybrid system

crystal structure

protein localization

neuropathology

DNA polymorphism

side effect: SI, side effect

meningoencephalitis: SI, side effect

human

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human

nonhuman

**clinical trial**

**review**

priority journal

Drug Descriptors:

\*adaptor protein: EC, endogenous compound

\*amyloid precursor protein: EC, endogenous compound

amyloid beta protein: AE, adverse drug reaction

**amyloid beta protein: CT, clinical trial**

alpha secretase: EC, endogenous compound

gamma secretase: EC, endogenous compound

beta secretase: EC, endogenous compound

phosphotyrosine: EC, endogenous compound

adaptor protein x11: EC, endogenous compound

adaptor protein Fe65: EC, endogenous compound

stress activated protein kinase: EC, endogenous compound

**proteinase inhibitor: AE, adverse drug reaction**

tsukubaenolide: PD, pharmacology

rapamycin: PD, pharmacology

fusicoccin: PD, pharmacology

**protein inhibitor: CT, clinical trial**

**protein inhibitor: CM, drug comparison**

**protein inhibitor: PD, pharmacology**

cyclosporin: CM, drug comparison

unclassified drug

RN (amyloid beta protein) 109770-29-8; (phosphotyrosine) 21820-51-9; (stress  
activated protein kinase) 155215-87-5; (proteinase **inhibitor**)  
37205-61-1; (tsukubaenolide) 104987-11-3; (rapamycin) 53123-88-9;  
(fusicoccin) 20108-30-9; (cyclosporin) 79217-60-0

CN Fk506

nonhuman

**clinical trial**

**review**

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CN Fk506

AN 2000:807191 CAPLUS

DN 134:337145

ED Entered STN: 16 Nov 2000

TI Immunophilins: Switched on **protein binding** domains?

AU Ivery, Michael T. G.

CS Faculty of Pharmacy, University of Sydney, N.S.W. 2006, Australia

SO Medicinal Research Reviews (2000), 20(6), 452-484

CODEN: MRREDD; ISSN: 0198-6325

PB John Wiley &amp; Sons, Inc.

DT Journal; General Review

LA English

CC 6-0 (General Biochemistry)

Section cross-reference(s): 1, 7

AB A **review** with 129 refs. Peptidylprolyl isomerases (PPIases) are a group of cytosolic enzymes first characterized by their ability to catalyze the cis-trans isomerization of cis-peptidylprolyl bonds. Subsequently, some PPIases were also identified as the initial targets of the immunosuppressant drugs-cyclosporin A (CsA), FK506, and rapamycin-have been called immunophilins. Immunophilins have been found to be both widely distributed and abundantly expressed leading to suggestions that they may play a general role in cellular biochem. However, the nature of this role has been difficult to elucidate and is still controversial in **vivo**. A number of roles for these enzymes have been identified in vitro including the ability to catalyze the refolding of partly denatured proteins and stabilize multiprotein complexes such as Ca<sup>2+</sup> channels, inactive steroid receptor complexes, and receptor protein tyrosine kinases. Generally, these effects appear to depend on the ability of immunophilins to selectively bind to other proteins. This **review** will examine in detail exptl. and structural investigations of the mechanism of PPIase activity for both **FKBPs** and cyclophilins and suggest a mechanism for these enzymes, which depends on their ability to recognize a specific peptide conformation rather than sequence. Examination of structures of immunophilin-protein complexes will then be used to further suggest that the ability of these enzymes to recognize specific peptide conformations is central to the formation of these complexes and may constitute a general function of immunophilin enzymes. The binding of ligand to immunophilins will also be shown to stabilize specific conformations in surface loops of these proteins that are observed to play a critical role in a number of immunophilin-protein complexes suggesting that the immunophilins may constitute a class of ligand-triggered selective protein binders.

ST immunophilin **FKBP protein binding****review**

IT Proteins, specific or class

RL: BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); PROC (Process)

(FKBP (FK 506-binding protein); immunophilins: switched on **protein binding** domains)

IT Protein receptors

RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)

(binding; immunophilins: switched on **protein binding** domains)

IT Isomerization

(cis-trans; immunophilins: switched on **protein binding** domains)

IT Protein folding

(immunophilins: switched on **protein binding** domains)

IT Cyclophilins

Immunophilins

RL: BPR (Biological process); BSU (Biological study, unclassified); PRP

AN 2000:807191 CAPLUS

DN 134:337145

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IT Proteins, specific or class

RL: BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); PROC (Process)

(FKBP (FK 506-binding protein); immunophilins: switched on **protein binding** domains)

IT Protein receptors

RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)

(binding; immunophilins: switched on **protein binding** domains)

IT Isomerization

(cis-trans; immunophilins: switched on **protein binding** domains)

IT Protein folding

(immunophilins: switched on **protein binding** domains)

IT Cyclophilins

Immunophilins

RL: BPR (Biological process); BSU (Biological study, unclassified); PRP

(Properties); BIOL (Biological study); PROC (Process)  
(immunophilins: switched on **protein binding**  
domains)

IT Conformation  
(protein; immunophilins: switched on **protein binding**  
domains)

IT 95076-93-0, Peptidylprolyl isomerase  
RL: BPR (Biological process); BSU (Biological study, unclassified); PRP  
(Properties); BIOL (Biological study); PROC (Process)  
(immunophilins: switched on **protein binding**  
domains)

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- (50) Marks, A; Am J Physiol 1997, V41, PH597

(Properties); BIOL (Biological study); PROC (Process)  
(immunophilins: switched on **protein binding**  
domains)

IT Conformation  
(protein; immunophilins: switched on **protein binding**  
domains)

IT 95076-93-0, Peptidylprolyl isomerase  
RL: BPR (Biological process); BSU (Biological study, unclassified); PRP  
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